



## Summary of Studies Supporting USDA Product Licensure

Establishment Name	Diamond Animal Health, Inc.
USDA Vet Biologics Establishment Number	213
Product Code	9381.D0
True Name	DNA Immunostimulant
Tradenname(s) / Distributor or Subsidiary (if different from manufacturer)	Diamond Animal Health, Inc. Victrio - Bayer HealthCare LLC - Diamond Animal Health, Inc. Victrio - Bayer, Inc., Toronto, Canada Victrio - Bayer, S.A. Victrio - Elanco US, Inc. - Diamond Animal Health, Inc. Victrio - No distributor specified Zelnote - Bayer HealthCare LLC - Diamond Animal Health, Inc. Zelnote - Bayer, Inc., Toronto, Canada Zelnote - Bayer, S.A. Zelnote - Bayer, S.A. - Diamond Animal Health, Inc. Zelnote - Elanco US, Inc. - Diamond Animal Health, Inc.
Date of Compilation Summary	June 04, 2021

**Disclaimer: Do not use the following studies to compare one product to another. Slight differences in study design and execution can render the comparisons meaningless.**

<b>Study Type</b>	Efficacy
<b>Pertaining to</b>	Avian Pathogenic <i>Escherichia coli</i>
<b>Study Purpose</b>	To demonstrate efficacy in embryonated eggs
<b>Product Administration</b>	One dose administered <i>in ovo</i> to 18-day-old embryonated chicken eggs. Control groups administered diluent only.
<b>Study Animals</b>	Embryonated eggs were randomized into 3 groups: one product treated group and two control groups. Each group consisted of 20 trays with 80 eggs each. Each tray was hatched and the chicks placed into pens.
<b>Challenge Description</b>	Live avian pathogenic <i>E. coli</i> inoculum (APEC), administered by spray to eggs one day after treatment.
<b>Interval observed after challenge</b>	Hatch rate was determined on day 21 of incubation and chicks were observed for 7 days post hatch.
<b>Results</b>	The hatch rate was determined on day 21 of incubation and the newborn chick mortality was determined after the first week of life. Treatment group 1 was treated with diluent only and mock challenged with sterile broth. Treatment group 2 was treated with diluent only and challenged with APEC. Treatment group 3 was treated with one dose of product <i>in ovo</i> and challenged with APEC.  Data for each group by pen is tabulated on the next pages.
<b>USDA Approval Date</b>	4-Oct-2012

## Treatment Group 1

Hatcher 2 Tray ID	Pen ID	Number at E18	Number Hatched	% Mortality at Hatch	Number at Day 7	% Mortality Post-Hatch	% Cumulative Mortality
1	61	80	67	16.3	67	0.0	16.3
3	62	80	77	3.8	77	0.0	3.8
5	63	80	72	10.0	71	1.4	11.3
7	64	80	72	10.0	72	0.0	10.0
9	65	80	74	7.5	73	1.4	8.8
11	66	80	76	6.3	76	0.0	6.3
13	67	80	78	2.5	78	0.0	2.5
15	68	80	77	3.8	78	1.3	5.0
16	69	80	70	12.5	70	0.0	12.5
18	70	80	76	5.0	75	1.3	6.3
31	71	80	76	6.3	74	1.3	7.5
33	72	80	76	5.0	76	0.0	5.0
46	73	80	80	0.0	79	1.3	1.3
48	74	80	76	6.3	75	0.0	6.3
50	75	80	78	2.5	78	0.0	2.5
52	76	80	77	3.8	77	0.0	3.8
54	77	80	79	1.3	77	2.5	3.8
56	78	80	77	3.8	75	2.6	6.3
58	79	80	80	0.0	80	0.0	0.0
60	80	80	76	5.0	75	1.3	6.3

E18 is 18-day-old embryonated chicken eggs

## Treatment Group 2

Hatcher 1 Tray ID	Pen ID	Number at E18	Number Hatched	% Mortality at Hatch	Number at Day 7	% Mortality Post-Hatch	% Cumulative Mortality
1	1	80	62	22.5	51	17.7	36.3
6	5	80	72	10.0	62	13.9	22.5
8	9	80	66	17.5	58	12.1	27.5
12	12	80	74	7.5	65	12.2	18.8
15	13	80	66	17.5	48	27.3	40.0
17	16	80	42	47.5	34	19.0	57.5
20	20	80	63	21.3	53	15.9	33.8
23	22	80	69	13.8	56	18.8	30.0
25	27	80	67	16.3	58	13.4	27.5
29	28	80	64	20.0	49	23.4	38.8
31	31	80	65	18.8	56	13.8	30.0
36	35	80	70	12.5	62	11.4	22.5
37	37	80	51	36.3	44	13.7	45.0
42	40	80	62	22.5	53	14.5	33.8
45	45	80	63	21.3	51	19.0	36.3
47	46	80	69	13.8	55	20.3	31.3
50	49	80	62	22.5	47	24.2	41.3
53	54	80	61	23.8	53	13.1	33.8
56	56	80	65	18.8	44	32.3	45.0
60	60	80	65	18.8	54	16.9	32.5

E18 is 18-day-old embryonated chicken eggs

### Treatment Group 3

Hatcher 1 Tray ID	Pen ID	Number at E18	Number Hatched	% Mortality at Hatch	Number at Day 7	% Mortality Post-Hatch	% Cumulative Mortality
2	2	80	65	18.8	58	10.8	27.5
5	6	80	73	8.8	69	5.5	13.8
7	7	80	65	18.8	57	12.3	28.8
10	11	80	59	26.3	54	8.5	32.5
13	14	80	62	22.5	57	8.1	28.8
16	17	80	73	8.8	67	8.2	16.3
19	21	80	61	23.8	59	3.3	26.3
24	24	80	70	12.5	65	7.1	18.8
27	26	80	67	16.3	62	7.5	22.5
28	30	80	66	17.5	61	7.6	23.8
33	32	80	59	26.3	56	5.1	30.0
35	34	80	62	22.5	56	9.7	30.0
39	38	80	66	13.8	64	7.2	20.0
40	41	80	70	12.5	63	10.0	21.3
43	44	80	63	21.3	59	6.3	26.3
46	48	80	70	12.5	68	2.9	15.0
49	50	80	66	17.5	59	10.6	26.3
52	52	80	68	15.0	61	10.3	23.8
57	57	80	68	15.0	64	5.9	20.0
58	58	80	67	16.3	61	9.0	23.8

E18 is 18-day-old embryonated chicken eggs

<b>Study Type</b>	Efficacy
<b>Pertaining to</b>	Avian pathogenic <i>Escherichia coli</i>
<b>Study Purpose</b>	To demonstrate efficacy when the product is administered with a commercially available Marek's Disease Virus (MDV) vaccine (HVT/SB1) in embryonated eggs
<b>Product Administration</b>	One dose administered <i>in ovo</i> to 18-day-old embryonated eggs, with or without administration of a commercially available MDV vaccine (HVT/SB1). Control groups administered diluent only.
<b>Study Animals</b>	Embryonated eggs were randomized into 3 groups: one product treated group and two control groups. Each group consisted of 20 trays with 80 eggs each. Each tray was hatched and the chicks placed into pens.
<b>Challenge Description</b>	Live avian pathogenic <i>E. coli</i> inoculum (APEC), administered by spray to eggs one day after treatment.
<b>Interval observed after challenge</b>	Hatch rate was determined on day 21 of incubation and chicks were observed for 7 days post hatch.
<b>Results</b>	The hatch rate was determined on day 21 of incubation and after the first week of life, and the combined (cumulative) mortality was calculated. Treatment group 1 was treated with diluent only and mock challenged with sterile broth. Treatment group 2 was treated with diluent only and challenged with APEC. Treatment group 3 was treated with one dose of product <i>in ovo</i> and challenged with APEC. Treatment group 4 was treated with one dose of product and also administered one dose of commercially available HVT/SB1 MDV vaccine <i>in ovo</i> and challenged with APEC.  Data for each group by pen is tabulated on the next page.
<b>USDA Approval Date</b>	5-Feb-2014

### Treatment Group 1

Hatcher 2 Tray ID	Pen ID	Number at E18	Number Hatched	% Mortality at Hatch	Number Live at Day 7	% Mortality Post-Hatch	% Cumulative Mortality
1	61	80	70	12.5	70	0.0	12.5
3	62	80	74	7.5	71	4.1	11.3
5	63	80	61	23.8	58	4.9	27.5
7	64	80	67	16.3	62	7.5	22.5
9	65	80	77	3.8	76	1.3	5.0
11	66	80	73	8.8	73	0.0	8.8
13	67	80	68	15.0	67	1.5	16.3
15	68	80	75	6.3	75	0.0	6.3
16	69	80	74	7.5	73	1.4	8.8
18	70	80	70	12.5	70	0.0	12.5
31	71	80	72	10.0	70	2.8	12.5
33	72	80	72	10.0	69	4.2	13.8
46	73	80	70	12.5	69	1.4	13.8
48	74	80	71	11.3	71	0.0	11.3
50	75	80	71	11.3	71	0.0	11.3
52	76	80	70	12.5	68	2.9	15.0
54	77	80	76	5.0	76	0.0	5.0
56	78	80	77	3.8	77	0.0	3.8
58	79	80	75	6.3	73	2.7	8.8
60	80	80	74	7.5	74	0.0	7.5

E18 is 18-day-old embryonated chicken eggs

## Treatment Group 2

Hatcher 1 Tray ID	Pen ID	Number at E18	Number Hatched	% Mortality at Hatch	Number Live at Day 7	% Mortality Post-Hatch	% Cumulative Mortality
2	2	80	65	18.8	45	30.8	43.8
6	6	80	68	15.0	51	25.0	36.3
8	8	80	66	17.5	49	25.8	38.8
11	10	80	64	20.0	43	32.8	46.3
14	14	80	57	28.8	37	35.1	53.8
18	18	80	61	23.8	47	23.0	41.3
19	21	80	70	12.5	51	27.1	36.3
22	24	80	64	20.0	45	29.7	43.8
25	26	80	68	15.0	47	30.9	41.3
29	28	80	64	20.0	35	45.3	56.3
31	31	80	68	15.0	51	25.0	36.3
35	35	80	65	18.8	53	18.5	33.8
38	37	80	61	23.8	43	29.5	46.3
41	40	80	57	28.8	45	21.1	43.8
43	43	80	66	17.5	51	22.7	36.3
46	47	80	64	20.0	44	31.3	45.0
49	49	80	61	23.8	44	27.9	45.0
54	52	80	65	18.8	55	15.4	31.3
56	55	80	68	15.0	51	25.0	36.3
58	58	80	60	25.0	38	36.7	52.5

E18 is 18-day-old embryonated chicken eggs

### Treatment Group 3

Hatcher 1 Tray ID	Pen ID	Number at E18	Number Hatched	% Mortality at Hatch	Number Live at Day 7	% Mortality Post-Hatch	% Cumulative Mortality
1	1	80	58	27.5	50	13.8	37.5
4	4	80	68	15.0	59	13.2	26.3
9	9	80	64	20.0	53	17.2	33.8
12	11	80	49	38.8	37	24.5	53.8
13	15	80	65	18.8	55	15.4	31.3
17	16	80	68	15.0	59	13.2	26.3
21	20	80	71	11.3	61	14.1	23.8
24	23	80	58	27.5	51	12.1	36.3
27	27	80	73	8.8	65	11.0	18.8
28	29	80	70	12.5	56	20.0	30.0
32	32	80	67	16.3	60	10.4	25.0
36	36	80	55	31.3	47	14.5	41.3
39	38	80	63	21.3	50	20.6	37.5
42	41	80	66	17.5	55	16.7	31.3
44	45	80	66	17.5	49	25.8	38.8
48	48	80	62	22.5	57	8.1	28.8
51	50	80	68	15.0	61	10.3	23.8
53	54	80	66	17.5	62	6.1	22.5
55	56	80	62	22.5	54	12.9	32.5
60	59	80	61	23.8	46	24.6	42.5

E18 is 18-day-old embryonated chicken eggs

### Treatment Group 4

Hatcher 1 Tray ID	Pen ID	Number at E18	Number Hatched	% Mortality at Hatch	Number Live at Day 7	% Mortality Post-Hatch	% Cumulative Mortality
3	3	80	51	36.3	45	11.8	43.8
5	5	80	64	20.0	57	10.9	28.8
7	7	80	72	10.0	63	12.5	21.3
10	12	80	61	23.8	51	16.4	36.3
15	13	80	62	22.5	55	11.3	31.3
16	17	80	72	10.0	59	18.1	26.3
20	19	80	65	18.8	56	13.8	30.0
23	22	80	69	13.8	61	11.6	23.8
26	25	80	64	20.0	56	12.5	30.0
30	30	80	68	15.0	57	16.2	28.8
33	33	80	61	23.8	55	9.8	31.3
34	34	80	60	25.0	52	13.3	35.0
37	39	80	50	37.5	45	10.0	43.8
40	42	80	66	17.5	54	18.2	32.5
45	44	80	58	27.5	51	12.1	36.3
47	46	80	63	21.3	56	11.1	30.0
50	51	80	61	23.8	50	18.0	37.5
52	53	80	52	35.0	42	19.2	47.5
57	57	80	62	22.5	48	22.6	40.0
59	60	80	68	15.0	53	22.1	33.8

E18 is 18-day-old embryonated chicken eggs

<b>Study Type</b>	Efficacy
<b>Pertaining to</b>	ALL
<b>Study Purpose</b>	To demonstrate efficacy when the product is administered with a commercially available Marek's Disease Virus (MDV) vaccine (HVT/SB1) in embryonated eggs
<b>Product Administration</b>	One dose administered <i>in ovo</i> to 18-day-old embryonated eggs with administration of a commercially available MDV vaccine (HVT/SB1). Control groups administered diluent only.
<b>Study Animals</b>	Embryonated eggs were randomized to 5 groups. 48 eggs were assigned to group T1 and 130 eggs assigned each to groups T2 to T5.
<b>Challenge Description</b>	Very virulent Marek's Disease Virus (vvMDV), strain RB-1B, administered on day 5 post-hatch to 100 chicks from each group T2 to T5.
<b>Interval observed after challenge</b>	Clinical observations were conducted on all chickens for 49 days post-hatch and all were observed at time of death for lesions associated with Marek's Disease.
<b>Results</b>	<p>Treatment group 1 was treated <i>in ovo</i> with diluent only on day 18 of incubation and the chicks were not challenged on day 5 post-hatch.</p> <p>Treatment group 2 was treated <i>in ovo</i> with one dose of a commercially available MDV vaccine HVT/SB1 on day 18 of incubation and the chicks were challenged on day 5 post-hatch. Treatment group 3 was treated <i>in ovo</i> with one dose of MDV vaccine HVT/SB1 and one dose of product on day 18 of incubation and the chicks were challenged on day 5 post-hatch.</p> <p>Treatment group 4 was treated <i>in ovo</i> with one dose of MDV control vaccine HVT on day 18 of incubation and the chicks were challenged on day 5 post-hatch. Treatment group 5 was treated <i>in ovo</i> with diluent only on day 18 of incubation and the chicks were challenged on day 5 post-hatch.</p> <p>Marek's lesions observations by isolator are tabulated on the next page.</p>
<b>USDA Approval</b>	28-Aug-2014

### Daily Mortalities – Control Groups

Study Day (Post-hatch)	Event	T1				T4				T5			
		Daily Mortality			Total Live	Daily Mortality			Total Live	Daily Mortality			Total Live
		Rm 127	Rm 128	Total Dead		Rm 127	Rm 128	Total Dead		Rm 127	Rm 128	Total Dead	
0 (24Jan14)	Hatch / Placement	22	22	0	44	60	60	0	120	59	60	0	119
1		0	0	0	44	0	0	0	120	0	0	0	119
2		0	0	0	44	1	0	1	119	0	0	0	119
3		0	0	0	44	0	0	0	119	0	0	0	119
4		0	0	0	44	0	0	0	119	1	0	1	118
5 (29Jan14)	Challenge	0	0	0	44	0	0	0	100 <sup>2</sup>	0	0	0	100 <sup>2</sup>
6		0	0	0	44	0	0	0	100	0	0	0	100
7		0	0	0	44	0	0	0	100	0	0	0	100
8		0	0	0	44	0	0	0	100	0	0	0	100
9		0	0	0	44	0	0	0	100	0	0	0	100
10		0	0	0	44	0	0	0	100	0	0	0	100
11		0	0	0	44	0	0	0	100	1	0	1	99
12		0	0	0	44	0	0	0	100	0	0	0	99
13		0	0	0	44	0	0	0	100	0	0	0	99
14		0	0	0	44	0	0	0	100	1	0	1	98
15		0	0	0	44	2	1	3	97	3	3	6	92
16		0	0	0	44	1	1	2	95	1	1	2	90
17		2 <sup>1</sup>	2 <sup>1</sup>	4 <sup>1</sup>	40	2	3	5	90	1	0	1	89
18		0	0	0	40	0	0	0	90	0	0	0	89
19		0	0	0	40	0	0	0	90	0	0	0	89
20		0	0	0	40	0	0	0	90	0	0	0	89
21		0	0	0	40	0	0	0	90	0	0	0	89
22		0	0	0	40	0	0	0	90	0	0	0	89
23		0	0	0	40	0	0	0	90	0	0	0	89
24		0	0	0	40	0	0	0	90	0	0	0	89
25		0	0	0	40	0	0	0	90	0	0	0	89
26		0	0	0	40	0	0	0	90	1	0	1	88
27		0	0	0	40	0	0	0	90	0	0	0	88
28		0	0	0	40	0	0	0	90	1	0	1	87
29		0	0	0	40	0	0	0	90	0	0	0	87
30		0	0	0	40	2	0	2	88	0	1	1	86
31		0	0	0	40	0	3	3	85	1	0	1	85
32		0	0	0	40	1	1	2	83	1	4	5	80
33		0	0	0	40	3	2	5	78	1	1	2	78
34		0	0	0	40	1	2	3	75	2	1	3	75
35		0	0	0	40	3	1	4	71	3	1	4	71
36		0	0	0	40	1	4	5	66	3	1	4	67
37		0	0	0	40	0	1	1	65	1	3	4	63
38		0	0	0	40	1	0	1	64	3	2	5	58
39		0	0	0	40	4	2	6	58	3	2	5	53
40		0	0	0	40	2	1	3	55	1	2	3	50
41		0	0	0	40	0	2	2	53	2	2	4	46
42		0	0	0	40	2	2	4	49	1	9	10	36
43		0	0	0	40	0	1	1	48	3	1	4	32
44		0	0	0	40	5	1	6	42	2	0	2	30
45		0	0	0	40	1	1	2	40	1	3	4	26
46		0	0	0	40	0	5	5	35	0	0	0	26
47		0	0	0	40	3	1	4	31	2	1	3	23
48		0	0	0	40	0	2	2	29	3	0	3	20
49 (14Mar14)	Necropsy	0	0	0	40 (0) <sup>3</sup>	0	0	0	29 (14) <sup>3</sup>	0	1	0	20 (20) <sup>3</sup>

<sup>1</sup>Birds removed due to over-crowding; <sup>2</sup>Only 100 birds from treatment group were challenged; <sup>3</sup># MD+ AT NECROPSY

### Daily Mortalities – Test Groups

Study Day (Post-hatch)	Event	T2				T3			
		Daily Mortality			Total Live	Daily Mortality			Total Live
		Rm 127	Rm 128	Total Dead		Rm 127	Rm 128	Total Dead	
0 (24Jan14)	Hatch / Placement	60	60	0	120	57	57	0	114
1		0	0	0	120	0	0	0	114
2		0	0	0	120	0	0	0	114
3		0	0	0	120	0	0	0	114
4		0	0	0	120	0	0	0	114
5 (29Jan14)	Challenge	0	0	0	100 <sup>1</sup>	0	0	0	100 <sup>1</sup>
6		0	0	0	100	0	0	0	100
7		0	0	0	100	0	0	0	100
8		0	0	0	100	0	0	0	100
9		0	0	0	100	0	0	0	100
10		0	0	0	100	0	0	0	100
11		0	0	0	100	0	0	0	100
12		0	0	0	100	0	0	0	100
13		0	0	0	100	0	0	0	100
14		1	0	1	99	0	0	0	100
15		1	0	1	98	1	0	1	99
16		0	0	0	98	0	2	2	97
17		3	0	3	95	0	0	0	97
18		0	0	0	95	0	0	0	97
19		0	0	0	95	0	0	0	97
20		0	0	0	95	0	0	0	97
21		0	0	0	95	0	0	0	97
22		0	0	0	95	0	0	0	97
23		0	0	0	95	0	0	0	97
24		0	0	0	95	0	0	0	97
25		0	0	0	95	0	0	0	97
26		0	0	0	95	0	1	1	96
27		0	0	0	95	0	0	0	96
28		0	2	2	93	0	1	1	95
29		2	0	2	91	1	0	1	94
30		0	0	0	91	0	1	1	93
31		1	1	2	89	0	0	0	93
32		0	2	2	87	1	2	3	90
33		1	2	3	84	0	0	0	90
34		2	1	3	81	2	2	4	86
35		1	2	3	78	3	2	5	81
36		1	3	4	74	2	0	2	79
37		0	2	2	72	0	1	1	78
38		2	0	2	70	0	1	1	77
39		3	3	6	64	1	2	3	74
40		1	4	5	59	1	0	1	73
41		3	0	3	56	0	1	1	72
42		0	1	1	55	2	1	3	69
43		3	0	3	52	1	0	1	68
44		0	0	0	52	0	0	0	68
45		0	1	1	51	0	0	0	68
46		1	0	1	50	0	0	0	68
47		1	1	2	48	1	0	1	67
48		2	0	2	46	1	1	2	65
49 (14Mar14)	Necropsy	0	0	0	46 (17) <sup>2</sup>	1	0	0	65 (10) <sup>2</sup>

<sup>1</sup>Only 100 birds from treatment group were challenged; <sup>2</sup># MD+ at Necropsy

<b>Study Type</b>	Efficacy																		
<b>Pertaining to</b>	DNA Immunostimulant																		
<b>Study Purpose</b>	Efficacy against bovine respiratory disease due to <i>Mannheimia haemolytica</i>																		
<b>Product Administration</b>	One dose administered by IM route at 24 hours <u>after</u> the time of challenge. Control group administered diluent only.																		
<b>Study Animals</b>	80 Holstein steers of average age 3.7 months; randomized into 2 groups of 40 calves each.																		
<b>Challenge Description</b>	All calves challenged with live <i>M. haemolytica</i>																		
<b>Interval observed after challenge</b>	Observed daily for 5 days after challenge. Lungs were evaluated on Day 5.																		
<b>Results</b>	<p><u>Mortality:</u> The deaths prior to Day 5 were: 1/40 in Treated group; 8/40 in Control group. All deaths were diagnosed as related to fibrinous bronchopneumonia (severe bovine respiratory disease).</p> <p><u>Lung scores:</u> The percent of lung mass that was abnormal (consolidated) was calculated/scored for every animal. For animals that died prior to Day 5, the lung score was not included in the analysis.</p> <p>5-number summary for lung consolidation:</p> <table border="1"> <thead> <tr> <th><b>Treatment</b></th> <th><b>Minimum</b></th> <th><b>Q<sub>1</sub></b></th> <th><b>Median</b></th> <th><b>Q<sub>3</sub></b></th> <th><b>Maximum</b></th> </tr> </thead> <tbody> <tr> <td>Controls</td> <td>1%</td> <td>10%</td> <td>14%</td> <td>29%</td> <td>48%</td> </tr> <tr> <td>Treated</td> <td>1%</td> <td>6%</td> <td>11%</td> <td>22%</td> <td>61%</td> </tr> </tbody> </table> <p>Raw data shown on attached page. The animals that died prior to Day 5 are marked with an asterisk (*).</p>	<b>Treatment</b>	<b>Minimum</b>	<b>Q<sub>1</sub></b>	<b>Median</b>	<b>Q<sub>3</sub></b>	<b>Maximum</b>	Controls	1%	10%	14%	29%	48%	Treated	1%	6%	11%	22%	61%
<b>Treatment</b>	<b>Minimum</b>	<b>Q<sub>1</sub></b>	<b>Median</b>	<b>Q<sub>3</sub></b>	<b>Maximum</b>														
Controls	1%	10%	14%	29%	48%														
Treated	1%	6%	11%	22%	61%														
<b>USDA Approval Date</b>	27-Jan-2014																		

**Lung consolidation scores (%), in order of rank:**

<b>Treated</b>	<b>Control</b>
1%	1%
1%	2%
2%	5%
2%	7%
3%	8%
3%	8%
3%	9%
3%	9%
3%	10%
6%	10%
6%	11%
7%	11%
8%	11%
8%	13%
9%	13%
10%	14%
11%	15%
11%	16%
11%	17%
11%	19%
11%	21%
13%	22%
15%	23%
15%	29%
17%	29%
18%	31%
19%	38%
20%	39%
22%	40%
23%	44%
26%	47%
28%	48%
29%	49% *
32%	51% *
33%	52% *
38%	54% *
38%	55% *
46% *	56% *
56%	57% *
61%	80% *

**\* death prior to Day 5**

<b>Study Type</b>	Efficacy																		
<b>Pertaining to</b>	DNA Immunostimulant																		
<b>Study Purpose</b>	Efficacy against bovine respiratory disease due to <i>Mannheimia haemolytica</i>																		
<b>Product Administration</b>	One dose administered by intranasal route <u>at the time of</u> challenge, utilizing mucosal atomization device. Control group administered diluent only via IM route.																		
<b>Study Animals</b>	64 Holstein steers of 4-6 months of age; randomized into 2 groups of 32 calves each.																		
<b>Challenge Description</b>	All calves challenged with live <i>M. haemolytica</i>																		
<b>Interval observed after challenge</b>	Observed daily for 5 days. Lungs were evaluated on day 5.																		
<b>Results</b>	<p>The deaths prior to Day 5 were:  1/32 in Treated group  9/32 in Control group  All deaths were diagnosed as related to severe bovine respiratory disease.</p> <p>The percent of lung mass that was abnormal (consolidated) was calculated/scored for every animal. For animals that died prior to Day 5, the lung score is not included in the 5 number summary.</p> <p>5 number summary for lung consolidation:</p> <table border="1"> <thead> <tr> <th><b>Treatment</b></th> <th><b>Minimum</b></th> <th><b>Q<sub>1</sub></b></th> <th><b>Median</b></th> <th><b>Q<sub>3</sub></b></th> <th><b>Maximum</b></th> </tr> </thead> <tbody> <tr> <td>Controls</td> <td>9%</td> <td>20%</td> <td>30%</td> <td>41%</td> <td>47%</td> </tr> <tr> <td>Treated</td> <td>9%</td> <td>20%</td> <td>26%</td> <td>31%</td> <td>52%</td> </tr> </tbody> </table> <p>Raw data shown on attached page. The animals that died prior to Day 5 are marked with an asterisk (*).</p>	<b>Treatment</b>	<b>Minimum</b>	<b>Q<sub>1</sub></b>	<b>Median</b>	<b>Q<sub>3</sub></b>	<b>Maximum</b>	Controls	9%	20%	30%	41%	47%	Treated	9%	20%	26%	31%	52%
<b>Treatment</b>	<b>Minimum</b>	<b>Q<sub>1</sub></b>	<b>Median</b>	<b>Q<sub>3</sub></b>	<b>Maximum</b>														
Controls	9%	20%	30%	41%	47%														
Treated	9%	20%	26%	31%	52%														
<b>USDA Approval Date</b>	1-Jun-2016																		

**Lung consolidation scores (%), in order of rank:**

<b>Treated</b>	<b>Control</b>
9%	9%
13%	10%
15%	12%
16%	17%
17%	19%
17%	19%
18%	20%
20%	21%
21%	28%
22%	29%
23%	29%
24%	30%
25%	32%
26%	35%
26%	37%
26%	40%
27%	41%
27%	41%
27%	42%
28%	44%
29%	45%
30%	46% *
30%	46%
31%	47%
32%	57% *
32%	58% *
37%	59% *
43%	63% *
45%	65% *
49%	68% *
52%	76% *
73% *	83% *

**\* death prior to Day 5**

<b>Study Type</b>	Efficacy																		
<b>Pertaining to</b>	<i>Mannheimia haemolytica</i>																		
<b>Study Purpose</b>	Efficacy against bovine respiratory disease																		
<b>Product Administration</b>	One dose administered by IM route <u>at the time of challenge</u> . Control group administered diluent only																		
<b>Study Animals</b>	64 Holstein steers of 3-4 months of age; randomized into 2 groups of 32 calves each																		
<b>Challenge Description</b>	live <i>M. haemolytica</i> inoculum																		
<b>Interval observed after challenge</b>	Observed daily for 5 days. Lungs were evaluated 5 days after challenge.																		
<b>Results</b>	<p>The percent of lung mass that was abnormal (consolidated) was calculated/scored for every animal. For animals that died prior to Day 5, the necropsy lung score was not included in the analysis.</p> <p>5 number summary for lung consolidation:</p> <table border="1"> <thead> <tr> <th><b>Treatment</b></th> <th><b>Minimum</b></th> <th><b>Q<sub>1</sub></b></th> <th><b>Median</b></th> <th><b>Q<sub>3</sub></b></th> <th><b>Maximum</b></th> </tr> </thead> <tbody> <tr> <td>Controls</td> <td>0%</td> <td>6%</td> <td>10%</td> <td>15%</td> <td>33%</td> </tr> <tr> <td>Treated</td> <td>0%</td> <td>1%</td> <td>4%</td> <td>10%</td> <td>22%</td> </tr> </tbody> </table> <p>Raw data shown on attached page. The animals that died prior to Day 5 are marked with an asterisk (*).</p> <p>The deaths prior to Day 5 were: 1/32 in Treated group; 1/32 in Control group. Diagnosis was severe peritonitis for calf in Treated group and severe bovine respiratory disease for calf in Control group.</p>	<b>Treatment</b>	<b>Minimum</b>	<b>Q<sub>1</sub></b>	<b>Median</b>	<b>Q<sub>3</sub></b>	<b>Maximum</b>	Controls	0%	6%	10%	15%	33%	Treated	0%	1%	4%	10%	22%
<b>Treatment</b>	<b>Minimum</b>	<b>Q<sub>1</sub></b>	<b>Median</b>	<b>Q<sub>3</sub></b>	<b>Maximum</b>														
Controls	0%	6%	10%	15%	33%														
Treated	0%	1%	4%	10%	22%														
<b>USDA Approval Date</b>	28-Feb-2013																		

**Lung consolidation scores (%), in order of rank:**

<b>Treated</b>	<b>Control</b>
0%	0%
0%	0%
1%	3%
1%	3%
1%	3%
1%	4%
1%	6%
1%	6%
2%	6%
2%	7%
3%	7%
3%	7%
3% *	8%
4%	8%
4%	10%
4%	10%
4%	10%
5%	10%
5%	10%
6%	11%
8%	13%
9%	14%
10%	15%
10%	15%
10%	18%
11%	18%
12%	21%
13%	23%
13%	27%
15%	29%
18%	33%
22%	34% *

**\* death prior to Day 5**

<b>Study Type</b>	Safety
<b>Pertaining to</b>	ALL
<b>Study Purpose</b>	Demonstrate safety of product under field conditions.
<b>Product Administration</b>	One dose administered by IM route.
<b>Study Animals</b>	614 steers and heifers ranging in age from 3 months to greater than 6 months at 4 sites in Nebraska, Indiana (2 sites), and Missouri. Approximately one-third of the population was of the minimum age of 3 months.
<b>Challenge Description</b>	NA
<b>Interval observed after challenge</b>	All animals were observed for 21 days after treatment. The injection site was palpated on day 3 or 4 after treatment.
<b>Results</b>	<p>No injection site lesions were observed.</p> <p>No adverse events were found attributable to the product per the investigators.</p> <p>There were a total of 51 adverse events which occurred at two of the sites, the majority (47/51) of these were determined to be the result of sequelae from Bovine Respiratory Disease on clinical signs. Two additional events were determined to be the result of either abdominal pain (due to bloat) or corneal oedema/blepharospasm (due to corneal injury). In addition, two animals died during the study and necropsy findings indicated the cause of death was tracheal edema/collapse syndrome or fibrinous bronchopneumonia. None of these adverse events were ascribed by the co-operators (investigators) to the experimental product.</p>
<b>USDA Approval Date</b>	24-Apr-2014

<b>Study Type</b>	Safety
<b>Pertaining to</b>	All
<b>Study Purpose</b>	Safety by intranasal route in cattle
<b>Product Administration</b>	
<b>Study Animals</b>	
<b>Challenge Description</b>	
<b>Interval observed after challenge</b>	
<b>Results</b>	Study data are not available

<b>Study Type</b>	Safety
<b>Pertaining to</b>	ALL
<b>Study Purpose</b>	To demonstrate safety of product under field conditions.
<b>Product Administration</b>	One dose administered by <i>in ovo</i> route.
<b>Study Animals</b>	183,082 eggs at three hatcheries in Georgia, Texas, and Mississippi were treated with Product Code 9381.D0 at 18 to 19 days of incubation. 92,640 control eggs were followed concurrently. 153,600 chicks from the treated eggs were placed in six typical grow-out houses. 76,800 control chicks were placed in three typical grow-out houses. The grow-out farms were located in South Carolina, Texas, and Mississippi. Treatment group T1 and Treatment group T2 received product administered with a commercially available MDV vaccine. Treatment group T3 received the commercially available MDV vaccine only.
<b>Challenge Description</b>	NA
<b>Interval observed after challenge</b>	Hatch rate was observed at all three hatcheries and all chickens were observed for 21 days after placement.
<b>Results</b>	The hatch rate and post-placement mortality rate at 21 days are tabulated by site and treatment group on the next page.  There were no treatment-related adverse events noted at any of the test sites.
<b>USDA Approval Date</b>	23-Apr-2014

**Hatch rate and post-placement mortality by site and treatment group.**

<b>Site &amp; Treatment Group</b>	<b>Total number embryonated eggs treated</b>	<b>Number of chicks hatched (% hatched)</b>	<b>Number of chicks placed, based on grow-out house capacity</b>	<b>Number of chicks alive at 21 days post-placement (% chicks alive)</b>
Site A, T1	36,912	34,900 (94.6%)	29,500	28,845 (97.8%)
Site A, T2	36,846	34,600 (93.9%)	29,500	29,026 (98.4%)
Site A, T3	36,796	34,700 (94.3%)	29,500	29,176 (98.9%)
Site B, T1	26,868	26,817 (98.8%)	24,200	24,067 (99.5%)
Site B, T2	27,937	26,362 (94.4%)	24,200	24,076 (99.5%)
Site B, T3	26,996	26,314 (97.5%)	24,200	24,043 (99.4%)
Site C, T1	27,494	26,387 (96.0%)	23,100	22,869 (99.0%)
Site C, T2	27,025	25,830 (95.6%)	23,100	22,872 (99.0%)
Site C, T3	28,848	27,719 (96.1%)	23,100	22,782 (98.6%)